

**UNITED STATES DISTRICT COURT  
DISTRICT OF MINNESOTA**

In re BAYCOL PRODUCTS LITIGATION	:	MDL No. 1431
	:	(MJD)
This Document Relates to:	:	
	:	
<i>All Actions</i>	:	
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**DEFENDANTS' MEMORANDUM IN SUPPORT OF THEIR MOTION  
TO EXCLUDE EXPERT TESTIMONY OF HARLAND AUSTIN**

Dr. Harland Austin violated the scientific method by starting from the conclusion he wanted to reach and then manipulating data to obtain his desired result. Dr. Austin's work involved an analysis of the PacifiCare study, a cohort epidemiological study conducted for Bayer to evaluate the risk of myopathy and rhabdomyolysis associated with the use of statins alone (monotherapy) and in conjunction with the use of gemfibrozil (combination therapy). This type of results-oriented analysis is inadmissible as expert testimony. *See Sorensen v. Shaklee Corp.*, 31 F.3d 638, 649 (8th Cir. 1994); *see also Mitchell v. Gencorp, Inc.*, 165 F.3d 778, 783 (10th Cir. 1999); *Claar v. Burlington N. R.R. Co.*, 29 F.3d 499, 502-03 (9th Cir. 1994). This Court should exclude Dr. Austin's testimony regarding the PacifiCare study, and his conclusions about the relative risk of Baycol use arising from his analysis of that study.

Further, Dr. Austin's opinions regarding Baycol monotherapy and combination therapy are inadmissible because they are based upon comparative adverse event reporting data. Report of Harland Austin (Ex. A) ¶ 26. In particular, he has testified that "Baycol monotherapy is associated with a higher rate of occurrence of

rhabdomyolysis than is monotherapy on other statins” and that there is “no credible explanation, other than causal” for this association. *Id.* Dr. Austin reaches this conclusion despite his admission that there are biases in the AER data — biases that he did nothing to eliminate and simply ignores. Such AER data cannot form the basis of an expert’s opinion on causation. *See, e.g., McClain v. Metabolife Int’l, Inc.*, 401 F.3d 1233, 1250 (11th Cir. 2005) (reversing jury verdict because expert testimony was based upon AERs and other unreliable evidence). Thus, Dr. Austin’s opinions regarding Baycol monotherapy are inadmissible.

## **BACKGROUND**

Dr. Austin is a biostatistician and professor of epidemiology at the Emory University School of Public Health in Atlanta, Georgia. Austin Rep. (Ex. A) ¶ 1. He was retained by the PSC primarily to evaluate the epidemiologic and statistical method of the PacifiCare study. *Id.* ¶ 13. See Motion to Exclude Expert Testimony of John Farquhar, Part I.B.1. (providing background on PacifiCare study). Dr. Austin did not review the underlying data from the PacifiCare study itself. As part of his analysis, he also reviewed comparative AER data that was primarily provided to him by the PSC.

Dr. Austin concedes that it was an “appropriate response” for Bayer to do a study like PacifiCare based on the signal raised by the AER data. Deposition of Harland Austin (Ex. B) at 174, 187-88. He claims, however, that the study has many “limitations” and therefore “underestimate[s] the association between monotherapy Baycol use and the risk of myopathy.” Austin Rep. (Ex. A) ¶ 14. Dr. Austin has “attempt[ed] to correct”

these “limitations” in the PacifiCare study by increasing the rate of myopathy associated with Baycol monotherapy by 40%. *Id.* ¶ 16; Austin Dep. (Ex. B) at 259-61. Based upon his re-calculation, Dr. Austin claims that PacifiCare actually shows an increased risk of myopathy associated with monotherapy Baycol. Austin Rep. (Ex. A) ¶ 16.

Dr. Austin, however, cannot provide any scientific basis for his 40% increase in the Baycol monotherapy rate. It appears that it was done solely to make the Baycol monotherapy rate look worse than that of other statins, based upon his “supposition” that there is an association between monotherapy Baycol and myopathy. *See* Austin Dep. (Ex. B) at 262. Dr. Austin’s opinions based on the PacifiCare study and comparative AER data are discussed further below.

***PacifiCare re-calculation:*** Dr. Austin claims that there are “many limitations” to the PacifiCare study, and that “its biases would tend to mask an increase in myopathy risk attributable to monotherapy Baycol.” Austin Rep. (Ex. A) ¶¶ 14, 16. Dr. Austin asserts that, as a result, he “attempt[ed] to correct the study findings for these biases.” *Id.* ¶ 16.

Dr. Austin “correct[ed]” the PacifiCare data by simply “inflat[ing]” the relative risk of Baycol monotherapy by 40%, while keeping the relative risk of the other statins constant. As Dr. Austin explained, he “inflate[d]the monotherapy Baycol RR [relative risk] by 30% for the failure of the investigators to eliminate false positives by medical record review and by 10% for the combination of non-differential misclassification of exposure, Baycol sampling, and that Baycol switching resulted in proportionately more Baycol person-time being contributed by subjects with a longer

history of HMG use than was so for the other statins.” *Id.* ¶ 74. As he succinctly describes it: “So I adjusted the values that started with just the adjustment for failure to do the correct analysis, and I added a little bit more.” Austin Dep. (Ex. B) at 260.

However, Dr. Austin did not “correct” or “inflate” the PacifiCare data for any other statin, even though many of the same supposed biases and limitations applied to those data as well. *See id.* at 262-63. The following exchange at Dr. Austin’s deposition is instructive on this point:

Q: Your false positives correction, do you just increase the rate for Baycol, or do you increase the rate for all the statins?

A: For Baycol.

Q: And why is that?

A: My interest was directed towards Baycol. You can multiply all the other ones by 1.1 as well.

Q: Well, I want to know why you, in your report, only increased the rate of Baycol because of this false positives concern and not the other statins.

A: Because my task was to answer the question does monotherapy with Baycol – is it – is it worse than monotherapy with the other statins. My attention was directed towards Baycol.

Q: By multiplying the Baycol figure by 1.1, did you make the Baycol monotherapy rate look worse?

A: Yes, I did.

Q: Okay, you could have multiplied the Pravachol monotherapy rate by 1.1 and held Baycol constant, right?

A: . . . . If basically the supposition here is that there is an association between Baycol and Baycol is – there’s an association between Baycol and the occurrence of myopathy and that because the study was done poorly, they missed that association. So multiplying it times the 1.1, that was my basis of multiplying it times the 1.1.

Q: So when you recalculated the PacifiCare data, you did so upon a supposition that there was a[n] association between Baycol and monotherapy and that it was higher for Baycol than the other statins?

A: In the context that if there were such a situation, that misclassification of exposure would obscure it, yes.

Q: Would the misclassification of exposure also obscure the situation where Zocor was higher than Baycol?

A: Yes.

Austin Dep. (Ex. B) at 261-63.

Dr. Austin failed to articulate any scientific basis in his report or at his deposition for increasing the Baycol rates by 40% and keeping the rates for all other statins unchanged. He further admitted that he could have done a “better” analysis had he analyzed the data instead of simply applying his re-calculation. Austin Dep. (Ex. B) at 264. He testified:

I think I’ve eliminated some of the bias [through the re-calculation]. I’ve made an attempt to eliminate some of the bias. But inherently, I – I – first of all, I would need the data myself to be able to do a better analysis. And certainly I can’t correct the flaws, the inherent flaws of that study. I made an attempt to do that. Do some flaws still remain? Probably.

*Id.*

***Comparative AER analysis:*** Dr. Austin reviewed “a number of tabulations of spontaneous reports of rhabdomyolysis and myopathy occurring among persons using” statins, including Baycol, at the request of plaintiffs’ counsel. Austin Report (Ex. A) ¶¶ 7, 9. With the exception of “one published report,” the tabulations Dr. Austin reviewed were “unpublished” and were provided to him by plaintiffs’ counsel. *Id.* ¶ 9. Each tabulation consists of data extracted from AERs submitted to the Food and Drug

Administration. *See id.* at Table 1. Dr. Austin also was provided with quarterly data pulled directly from the FDA's Adverse Event Reporting System. *Id.* ¶ 11.

Based on this AER data, Dr. Austin calculated a reporting rate ratio ("RRR") that compares the reporting rate for monotherapy Baycol to the aggregate reporting rate for other statins, and a proportional reporting ratio ("PRR"), which is a comparison of the proportion of adverse events for rhabdomyolysis reported for persons using Baycol divided by the corresponding proportion for persons using other statins. Austin Dep. (Ex. B) at 62-63; Austin Rep. (Ex. A) ¶¶ 17-26. Based on these RRR and PRR calculations, Dr. Austin concludes that Baycol caused a higher rate of rhabdomyolysis in monotherapy than other statins. *Id.* ¶ 26.

Even Dr. Austin allows, however, that this is possible only if one makes a number of assumptions, for which he had no evidence. The RRR, for example, is only valid "if the reporting rates are comparable across the statins." Austin Rep. (Ex. A) ¶ 19. In other words, the probability that rhabdomyolysis in Baycol users will be reported must be the same as the probability that rhabdomyolysis in users of other statins will be reported. Dr. Austin has pointed to no data to support this assumption, and in fact admits that "the assumption could be wrong." Austin Dep. (Ex. B) at 78. *See* Defendants' AER Motion, Part II (discussing some reasons reporting rates may vary among statins).

Dr. Austin attempts to correct for some of the flaws inherent in his RRR analysis by calculating the PRR for Baycol. Dr. Austin opines that the PRR has an advantage over the RRR because it corrects for certain reporting biases and "does not require an estimate of the number of prescriptions for the drugs of interest." Austin Rep.

(Ex. A) ¶ 22. For the PRR to be useful, however, Dr. Austin acknowledges that two assumptions must be made: (1) “the rate of all adverse events other than the one of interest” must be “the same for persons using drug X and drug Y” (the drugs being compared) and (2) “the ratio of probabilities of reporting the adverse event of interest for drug X to drug Y must equal the ratio of the probabilities of reporting all other adverse events for drugs X to drug Y.” *Id.* Once again, Dr. Austin has pointed to no data that would justify the assumptions required by his methodology. Nevertheless, because the RRR and PRR he calculates for Baycol are higher than those for other statins, Dr. Austin concludes that monotherapy Baycol is associated with a higher incidence rate of rhabdomyolysis than is monotherapy with other statins, and he speculates that the only “credible explanation” for such association is “causal.” *Id.* ¶ 26.

## ARGUMENT

### **I. DR. AUSTIN’S ANALYSIS AND OPINIONS REGARDING THE PACIFICARE DATA ARE INADMISSIBLE BECAUSE HIS METHODOLOGY IS THE ANTITHESIS OF THE SCIENTIFIC METHOD.**

Dr. Austin complains that the PacifiCare study was subject to bias. He then attempts to “correct” the study for those biases (but only as to Baycol) and to draw conclusions from his re-calculations. His method for supposedly “correcting” the PacifiCare data failed to follow the basic scientific method. “Scientific methodology today is based on generating hypotheses and testing them to see if they can be falsified; indeed, this methodology is what distinguishes science from other fields of human inquiry.” *Daubert*, 509 U.S. at 593 (quoting E. Green & C. Nesson, *Problems, Cases,*

*and Materials on Evidence* 645 (1983)). Instead of seeking to falsify a hypothesis, Dr. Austin skewed the PacifiCare data to fit his pre-conceived conclusion that Baycol monotherapy was “worse than monotherapy with the other statins.” Austin Dep. (Ex. B) at 262:2-5.

Dr. Austin’s re-calculation is based on the “supposition” that there is an association between monotherapy Baycol and myopathy. Austin Dep. (Ex. B) at 262-63. In other words, Dr. Austin works backwards from the result he assumes must be true.

The Eighth Circuit has rejected the conclusion-first approach that Dr. Austin employs. In *Sorensen v. Shaklee Corp.*, 31 F.3d 638 (8th Cir. 1994), the plaintiffs’ experts “reasoned from an end result in order to hypothesize what needed to be known but was not.” *Id.* at 649. A scientific opinion, by contrast, “reason[s] from known facts to reach a conclusion.” *Id.* By starting with their desired conclusion and working backward, the plaintiffs’ experts in that case “turn[ed] scientific analysis on its head.” *Id.*

Numerous other courts agree. For example, in *Claar*, 29 F.3d at 502-3, the Ninth Circuit, quoting *Daubert*, determined that “[i]n order to qualify as ‘scientific knowledge’ [as required by Rule 702], an inference must be derived by the scientific method.’ Coming to a firm conclusion first and then doing research to support it is the antithesis of this method.” Similarly, the Eleventh Circuit has noted that “[a] scientist who has a formed opinion as to the answer he is going to find before he even begins his research may be less objective than he needs to be in order to produce reliable scientific results.” *Perry v. U.S.*, 755 F.2d 888, 892 (11th Cir. 1985) (affirming the exclusion of an

epidemiologist who “had reached a conclusion as to the connection between encephalitis and the vaccine before commencing his research”); *see also Mitchell* 165 F.3d at 783 (same); *Viterbo v. Dow Chemical Co.*, 646 F. Supp. 1420, 1425 (E.D. Tex. 1986) (same).

Much like the experts who were excluded in *Sorensen* and *Claar*, Dr. Austin works backwards from his conclusion that Baycol was worse in monotherapy than the other statins. Dr. Austin then compounds that error by “inflat[ing]” only the relative risk of Baycol by 40%, while keeping the relative risks of the other statins constant. Dr. Austin, however, has not set forth any scientific basis for increasing the Baycol monotherapy rates (and no others) by 40%. His unsupported decision that a 40% increase will correct for any biases in the report is not sufficient. Nothing in the “Federal Rules of Evidence requires a district court to admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert.” *General Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997).

Further, Dr. Austin admits that he could have done a “better analysis” had he actually looked at the underlying PacifiCare data. Austin Dep. (Ex. B) at 264. By failing to do this more accurate analysis, and instead relying on guesswork to account for any potential biases in PacifiCare, Dr. Austin has failed to adhere to the same standards of intellectual rigor applied by pharmacoepidmiologists. *See Group Health Plan*, 344 F.3d at 760 (quoting *Rosen v. Ciba-Geigy Corp.*, 78 F.3d 316, 319 (7th Cir.), *cert. denied* 519 U.S. 819 (1996)) (“What is required is that when experts ‘testify in court they adhere to the same standards of intellectual rigor that are demanded in their professional work’”); *accord Kumho Tire Co.*, 526 U.S. at 152.

Dr. Austin's opinion, therefore, comes down to a cooking of the PacifiCare data to fit his pre-conceived conclusion that Baycol is worse than the other statins. This approach is not just "junk science," it is not science at all. His opinion should be excluded under both *Daubert* and Rule 702.

## **II. DR. AUSTIN'S TESTIMONY ON RELATIVE RISK IS INADMISSIBLE.**

AER data cannot be used to base an opinion on the relative risk of monotherapy Baycol as compared to other statins, as Dr. Austin has attempted to do here. *See* Defendants' AER Motion. Even Dr. Austin concedes that AERs have limitations, acknowledging that:

"[B]ecause spontaneous reports are not collected in the context of a formal, controlled study, they must be interpreted cautiously." Austin Rep. (Ex. A) ¶ 19; and

Due to potential reporting biases – including the secular reporting trend, the new drug bias, and the publicity bias – two medicines in the same drug class could be equally associated with a particular disease, but the AER reporting rates of the medicines might nonetheless differ. Austin Dep. (Ex. B) at 37-40.

When asked during his deposition what he had done "to eliminate bias as a possible explanation" for his conclusions, Dr. Austin responded that he "didn't do anything specifically because [he] didn't have anything but [the] tabulations" provided to him by plaintiffs' counsel. *Id.* at 74. Each of these tabulations consisted of data extracted from AERs, *see* Austin Rep. (Ex. A) at Table 1, and therefore are subject to the same set of caveats as the underlying AER data itself.

Despite this, Dr. Austin did nothing to attempt to eliminate the bias in such data, and instead cavalierly ignores the widely-accepted limitations of AER data to reach his opinion. This does not constitute a reliable method for determining the relative risk of Baycol.

Dr. Austin compounds these errors by using AER data to make novel and complicated RRR and PRR calculations, in a failed attempt to bolster his opinion on relative risk. The reliability of his RRR and PRR calculations is severely undercut by the unfounded assumptions upon which they are based, including:

- rhabdomyolysis reporting rates are comparable across all statins being compared, Austin Rep. (Ex. A) ¶ 19;
- the likelihood of reporting rhabdomyolysis is the same across all statins being compared, *id.* ¶ 22;
- the likelihood of reporting all other adverse events is the same for all statins being compared, *id.*; and
- “the rate of all adverse events other than the one of interest is the same” for all medicines being compared, *id.*

While acknowledging that these assumptions are necessary to his analysis and opinions, Dr. Austin points to no data justifying them. To the contrary, even though he acknowledges that the RRR is only valid “if the reporting rates are comparable across the statins,” Dr. Austin admits that this “assumption could be wrong.” Austin Rep. (Ex. A) ¶ 19; Austin Dep. (Ex. B) at 78. Similarly, with respect to his PRR calculation, he admits that assuming the rate of all adverse events (other than the one at interest) are the same constitutes a “strong assumption” and one he “would rather not make.” Austin Dep. (Ex. B) at 102-03.

Like a house of cards, Dr. Austin's opinion falls apart because its foundation is not sound. Dr. Austin ignores biases in AER data and then makes matters worse with complex PRR and RRR calculations that are built on dubious assumptions. As such, his opinion cannot withstand scrutiny and does not meet the "exacting" standard of reliability set forth in *Daubert*. "[T]o be scientifically reliable, comparisons between products must be made on the basis of formal scientific studies with control groups." Report of Brian L. Strom (Ex. C) ¶ 6. Dr. Austin's RRR and PRR analyses are not based on such evidence. Plaintiffs cannot carry their burden under *Daubert* to prove that the methodology used by Dr. Austin is generally accepted in the relevant field as a method for arriving at his conclusion on relative risk. *Blue Dane Simmental Corp. v. American Simmental Ass'n*, 178 F.3d 1035, 1040-41 (8th Cir. 1999) (excluding testimony of economics expert where no evidence that other economists used the model he used to support the conclusion he reached). Dr. Austin's testimony on relative risk should therefore be excluded by this Court.

### CONCLUSION

For these reasons, defendant Bayer respectfully submits that this Court should grant its motion to exclude Dr. Austin's proposed testimony about the relative risk of monotherapy Baycol based on his analysis of adverse event reports, and his re-calculation of the PacifiCare study.

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Respectfully submitted,

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